REMARKS

I. Claim Status

Claims 1, 5-14, 18-20, 22, 35, and 54 are pending.

Claim 2 has been canceled.

Claims 1, 8, 19, 35 and 54 have been amended.

II.

III. Rejection Under 35 U.S.C. §112

Claims 1, 5014, 18-20, 35 and 54 were rejected under 35 U.S.C. § 112, second, paragraph, as allegedly being indefinite. Applicants have amended the claims to replace the "δ" with "δ_2" as suggested in the Office Action.

IV. Rejection Under 35 U.S.C. § 103

Claims 1-5, 14, 18-20, and 35 stand rejected under 35 U.S.C. § 103(a) as allegedly being obvious by Lerman et al. (United States Patent No. 6,441,156) in view of Brown et al. (J. Biol. Chem. 273:25458-25465, 1998).

Lerman et al. disclose full length $\alpha_2\delta_2$ subunits, in particular Lerman et al. discloses SEQ ID NO.4, the full length human $\alpha_2\delta_2$ sequence which is the same as SEQ ID NO. 20 of the present application.

The difference between the present invention and the disclosure of Lerman is that the present invention, as claimed in amended claim 1, relates to $\alpha_2\delta_2$ subunits which are soluble rather than membrane bound and yet retain ligand binding activity. The objective problem to be solved, in view of Lerman, is how to provide a soluble $\alpha_2\delta_2$ subunit which retains ligand binding activity.

Amended claim 1 defines a specific C-terminal truncation into the δ_2 peptide of the $\alpha_2\delta_2$ subunit, the resulting truncated $\alpha_2\delta_2$ subunit retains the functional characteristics of the full-length or wild-type $\alpha_2\delta_2$ subunit from which it derives and is soluble.

This is not obvious to the skilled person from Lerman et al. alone as Lerman et al. do not teach nor suggest how to provide soluble forms of $\alpha_2\delta_2$ subunit. Accordingly, claim 1 is not obvious in view of Lerman et al.

Nor would it be obvious to derive the claimed invention from the combination of Lerman et al. with Brown et al. for the following reasons:

(a) Brown et al. relate to $\alpha_2\delta_1$ subunit not $\alpha_2\delta_2$ subunit, there is no indication in Brown et al. that the teaching, with respect to $\alpha_2\delta_1$ subunit, is applicable to $\alpha_2\delta_2$ subunit.

(b) Brown et al. disclose the preparation of 14 individual C-terminal truncated proteins of to $\alpha_2\delta_1$ subunit where the C-terminus is truncated, of these 14 only one (designated L) displayed partial solubility and good ligand binding ability. It is clear, from the statements of Brown et al. and from their failed results (set out in the quotations below), that there is no predictability to the production of a soluble form of $\alpha_2\delta_1$ subunit based on the general knowledge in the art at the publication date, i.e. the single transmembrane model. This model, as stated by Brown et al. proposes that the δ_1 transmembrane domain (Fig. 1 Brown et al.: Domain IV 1035-1060) is responsible for anchoring the protein to the membrane and that by merely removing this domain the skilled person will produce a soluble protein. This is clearly not the case as is apparent from the experimental results of Brown et al., all $\alpha_2\delta_1$ truncations other than L produced by Brown et al. in which the D transmembrane domain was truncated did not provide the requisite solubility of the protein: (Brown et al. page 25464 final paragraph). Brown et al. conclude that the provision of soluble $\alpha_2\delta_1$ is not predictable:

> "Our data broadly support the single transmembrane model of the A2D subunit, although the model cannot explain all the properties of mutant L and the heavily truncated forms of A2 (mutants B and C) which remain associated with the membrane", Brown et al. page 25465 final paragraph."

If the teaching of Brown et al. is that the provision of soluble $\alpha_2\delta_1$ is not predictable, then there is no reason why its teaching should be taken to indicate that the provision of a different protein, $\alpha_2\delta_2$, in soluble active form, should be predictable. One of ordinary skill in the art would find it most surprising and unexpected in view of Lerman et al. alone or the combination of Lerman et al. with Brown et al., that the sequences of amended claim 1 of the present invention is a soluble form of $\alpha_2\delta_2$. Accordingly, claim 1 is not rendered obvious.

Claims 2 - 15 are also patentable by virtue of their dependence on claim 1 and their requirement of the novel and non-obvious sequences.

IV. Conclusion

In view of the amendments and remarks made above Applicants believe that this application is in condition for allowance. Reconsideration and allowance of claims 1, 5-14, 18-20, 22, 35,and 54 is respectfully requested.

Respectfully submitted,

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